ADME NTP Study S0844 Methyleugenol Toxicokinetics

Sex/Species: male F344 rats.
Vehicle: intravenous, ethanol:Emulphor:saline (10:10:80).

CASRN 93-15-2

Radiolabeled with carbon-14 (position not specified); [^{14}C]Methyleugenol

Studies Performed:

Single 11.8 mg/kg intravenous dose to rats with sampling at 0, 1, 5,10, 15, 30, and 45 minutes as well as 1, 1.5, 2, 2.5, 3, 3.5, 4.5 and 6 hours postdose. (n = 3 with indwelling catheters)

Toxicokinetics:

Pharmacokinetic parameters for parent methyleugenol were likely calculated using Winnonlin software (Scientific Consulting, Inc., Apex, NC). Data were best fitted as a two compartment model (intravenous bolus dose). Parent methyleugenol was detected in blood by HPLC for the first 3.5-4 hours after administration and was not detectable after that point. Possible metabolites were detected in the blood through 30 minutes but never exceeded 0.1 % of the administered dose at any of the time-points analyzed.

Whole blood was counted for total radioactivity at each time point. After 6 hours, radioactvity was no longer detectable in the blood. For both parent and total radioactivity, the means for each time point to 6 hours were plotted in a figure and are not shown here.

Table 1 Pharmacokinetic Parameters of Intravenously Administered [^{14}C]-Methyleugenol (11.8 mg/kg, 120 uCi/kg).

Parameter (units)	V_{ss} L/kg	$t_{1/2}$ min	MRT Min	V_D L/kg	AUC ug/min/ml	CLs L/min/kg
Mean ± sem	9.02 ± 1.36	51.45 ± 5.18	61.76 ± 7.95	2.73 ± 0.42	81.83 ± 5.65	0.15 ± 0.01

Where:

V_{ss} is the steady-state apparent volume of distribution, the apparent volume into which the compound is distributed at steady state.

$t_{1/2}$ is the terminal half-life, the time it takes half the concentration of parent to be removed from the blood.

MRT is the mean residence time, the average time the drug resides in the body.

V_D is the volume of distribution, the apparent volume into which the compound is distributed.

AUC is the area under the curve, an expression of the amount of compound in the blood over time.

CL_s is the systemic body clearance, which describes the elimination of drug from the body by all processes.